

CLAIMS

What is claimed is:

1. A method to select altered peptide species for administration to a subject, said subject presenting a native ligand for which activation of an immune response against said native ligand is desired, comprising the steps of:
 - a. identifying a plurality of altered peptide species capable of eliciting an immune response to said native ligand;
 - b. selecting at least two altered peptide species wherein each altered peptide activates a population of T cells having a distinct T cell receptor V β recombination.
2. The method of claim 1, further comprising the step of administering said selected altered peptide species to said subject.
3. A method to select altered peptide species for administration to a member of a population of subjects having a given HLA-type, said population presenting a native ligand for which activation of an immune response against said native ligand is desired, comprising the steps of:
 - a. identifying a plurality of altered peptide species capable of eliciting an immune response to said native ligand; and
 - b. selecting two or more of said altered peptide species, wherein each of said altered peptide species activates a T cell having a distinct T cell receptor V β recombination in a sample representative of said population.
4. The method of claim 3, further comprising the step of administering said selected altered peptide species to said member.
5. The method of claim 3, wherein said HLA-type is HLA-A2.

6. The method of claims 1 or 3, comprising from at least 2 to 6 different altered peptide species.
7. The method of claims 1 or 3, comprising at least 3 different altered peptide species.
8. The method of claims 1 or 3, wherein at least one altered peptide species is covalently linked to one or more amino acids naturally contiguous to said native human ligand.
9. The method of claims 1 or 3, wherein said native ligand is a mammalian tumor epitope.
10. The method of claims 1 or 3, wherein said native ligand is a human viral antigen.
11. The method of claims 1 or 3, further comprising the step of formulating said selected altered peptides in a pharmaceutically acceptable carrier suitable for administration to humans.
- ~~12.~~ A composition comprising multiple peptide ligand species directed at a single native ligand, wherein at least two altered peptide species activate a different T cell clone from each other and the T cell receptor V β recombination of each of said activated T cell clones is different.
- ~~13.~~ A composition comprising two or more altered peptide species, wherein each of said two or more species is characterized by an ability to activate a different subpopulation of cytotoxic T lymphocytes (CTLs) against the same native ligand.

14. The composition of claims 12 or 13, comprising from at least 2 to 6 different peptide species.

15. The composition of claims 12 or 13, comprising at least 3 different peptide species.

16. The composition of claims 12 or 13, wherein at least one peptide species is covalently linked to one or more amino acids naturally contiguous to said native human ligand.

17. The composition of claim 13, wherein said altered peptide species activate said different subpopulations in one member of a selected population of subjects

18. The composition of claim 13, wherein said altered peptide species activate a different subpopulation in two or more members of said population of subjects.

19. The composition of claims 12 or 13, wherein said native ligand is a mammalian tumor epitope.

20. The composition of claims 12 or 13, wherein said native ligand is a human viral antigen.

21. The composition of claims 12 or 13, further comprising a pharmaceutically acceptable carrier.

22. A kit comprising:

- a. multiple peptide species directed at a single native ligand, wherein
 - i. a first peptide species activates a first T cell,

- ii. a second peptide species activates a second T cell,
and the T cell receptor V β recombination of said first T cell is different
from the T cell receptor V β recombination of said second T cell; and
- b. instructions for the co-administration of each of said peptides.

23. The kit of claim 22, wherein said selected peptide species are
packaged in combination.

24. The kit of claim 22, further comprising instructions to identify
subjects who exhibit a positive therapeutic response to the administration of said
multiple peptide ligand species.

~~25.~~ A method comprising the steps of:

- a. identifying a plurality of altered peptide species characterized by an
ability to elicit an immune response against the same native ligand;
- b. determining the T cell receptor V β recombination profile of the T
cell population activated by each of said identified altered peptide species in a
plurality of test subjects; and
- selecting at least two or more altered peptide species wherein each of said
altered peptide species activates T cell populations having distinct T cell receptor
V β recombinations in a majority of said test subjects.

26. The method of claim 25, wherein at least one of said selected
altered peptide species is more than said native antigen.

27. The method of claim 25, further comprising the step of
administering said selected altered peptide species to a subject having said native
antigen.

28. The method of claim 25, further comprising the step of packaging said selected altered peptide species in a form suitable for administration to a subject.

29. The method of claim 26, wherein said selected altered peptide species are packaged together.

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